Epitomes

Important Advances in Clinical Medicine

Chest Diseases

The Scientific Board of the California Medical Association presents the following inventory of items of progress in chest diseases. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, research workers or scholars to stay abreast of these items of progress in chest diseases that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Chest Diseases of the California Medical Association and the summaries were prepared under its direction.

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Strange Causes of Asthma

THE REVERSIBLE AIRWAYS obstruction of asthma can be induced by a large number of well-known provocative factors. These include exposure to familiar inhalant allergens, chemical or physical irritants, cold air, exercise, viral respiratory tract infection, emotional factors and, less commonly, dietary ingestion of food allergens. In some patients, intermittent soiling of the tracheobronchial tree by aspirated gastroesophageal contents can be an important cause of exacerbation of asthma. Not infrequently, attacks of asthma occur "out of the blue," with no apparent precipitant. Chronic cough can be a major (or the only) symptom of asthma, which, though not necessarily associated with reversible bronchospasm, can be documented by evidence of airways hyperreactivity when a patient is tested with certain inhalants ("cough-variant asthma"). Rarely, asthma may be mimicked by paroxysmal glottic obstruction that can be self-induced ("factitious asthma") or functional. Occasionally, true asthma may be provoked by strange or unusual causes that could escape the notice of patients and physicians unfamiliar with their asthmogenic potential. Some of these unusual or unsuspected causes of asthma include food additives, alcoholic beverages, certain drugs, iodinated radiographic contrast material, hemodialysis (due to acetate dialysate or complement-activation by cuprophane), domestic exposure to urea-formaldehyde foam insulation and a variety of occupational exposures (see below).

Food additives implicated in asthma include tartrazine dye, monosodium glutamate ("Chinese-restaurant asthma") and bisulfite preservatives, particularly when used in relatively high concentration as in restaurant foods, dried apricots or the processing of beer and wine; sulfur dioxide (SO_2) generated by the reaction of these sulfites with water provokes bronchospasm in some patients. Alcoholic beverages can induce bronchospasm due to adulterants in the beverage or, rarely, the ethanol itself. Commonly used drugs that can provoke asthma include aspirin and nonsteroidal anti-inflammatory agents; β-adrenergic antagonists (including timolol eye drops); drugs containing tartrazine (FD&C yellow No. 5) colorant additive; aqueous solutions of isoproterenol, isoetharine and metaproterenol containing metabisulfite preservative (from which liberated SO_2 could lead to "paradoxical bronchospasm"), and pancuronium bromide. Patients with asthma who have aspirin intolerance should be provided a list (available on request from the author, D. P. Tashkin, MD, Dept of Medicine, Center for the Health Sciences, UCLA School of Medicine, Los Angeles, CA 90024) of the more than 200 prescription and proprietary compounds that contain aspirin, most of which are combination products.

The prevalence of occupational asthma has risen dramatically in recent years due to the expanding list of asthmogenic substances used or generated in industry. In addition to gaseous irritants, animal proteins, grains, flour, gum, woods, drugs and enzymes, these substances include a number of low-molecular-weight compounds that may act as haptenes to produce immunologically mediated asthma: reactive dyes (including methyl blue in electrocardiographic ink); ethylenediamine (shellac, photographic chemicals); phthalic anhydride (paint, epoxy resins, meat wrapping); abietic acid (solder flux fumes leading to "colophony-induced asthma" in electronics workers); toluene diisocyanate (polyurethane foam, varnish), and other isocyanates

(automobile spray paint, laminates). Physicians need to be alert to the possibility that "strange" causes of asthma may lurk in increasingly complex workplaces.

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Bronchoscopy and Lasers

Fluorescence bronchoscopy is a sensitive method to locate small mucosal or intrabronchial cancer lesions not found on routine bronchoscopy in patients with positive sputum cytology studies and normal findings on chest x-ray films. Diagnosis is warranted at this early stage (stage 0, or $T_{IS}N_0M_0$) because resection may be expected to be 90% to 100% curative. With this method hematoporphyrin derivative, which is retained within cancer cells (of all histologic types, primary or metastatic), is injected intravenously. The fluorescence bronchoscope uses violet light (410 nm) from a krypton ion laser, conducted via a fine quartz fiber (0.4 nm) in its suction channel, to its tip. Fluorescing lesions are visualized with an image intensifier, are then brushed and a forceps biopsy done for specific diagnosis.

Photoradiation therapy for endobronchial tumors by bronchoscopy uses the photodynamic action of hematoporphyrin derivative within tumor cells to produce singlet oxygen when activated by red light (630 nm) conducted via a quartz fiber from an argon-pumped dye laser. Power is low (200 mW), and there is no immediate visible change or coagulating effect. Cell and cell membrane function are gradually impaired so that tumor cells die over the next 24 to 48 hours. Tumor debris is then removed by repeat-bronchoscopy, to open up the bronchus to its full extent. Even a totally occluded bronchus can be fully opened up, and an atelectatic lung, lobe or segment may be re-aerated. Methods of light application developed are effective and efficient; generally (80% to 90% of cases) only one treatment is required. There have been no complications during photoradiation treatment of obstructing endobronchial tumors. Photoradiation therapy for early bronchial cancer is potentially curative, and clinical trials are under way.

Photocoagulation therapy uses pulses of a beam of intense (20 to 40 W) infrared light (1,060 nm) from an Nd-YAG laser. Tumor tissue is thereby immediately coagulated by heating (50°C to 60°C), or can be vaporized (100°C) by higher power (40 to 90 W). Large obstructing tracheal and main bronchus tumors after coagulation can be sheared off by the tip of the rigid bronchoscope. Tumors and granulation tissue masses and fibrotic stenotic areas caused by an endotracheal tube or tracheostomy can be vaporized. The tip of the fiber must be carefully aimed to prevent penetration of the wall, hemorrhage and possible death.

These new advances in bronchoscopic laser therapy are effective and safe in experienced hands. Still to be documented are patient benefits in terms of survival, the duration of control of the tracheobronchial lesions and whether they recur, the degree of improved breathing and lessened cough and the prevention of recurrent respiratory tract infections and distal pneumonia.

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Drug Therapy for Pulmonary Hypertension

THE TREATMENT of pulmonary hypertension depends on its cause and includes such diverse measures as anticoagulant or fibrinolytic therapy for pulmonary embolic disease; oxygen, bronchodilators and pulmonary hygiene for patients with chronic obstructive pulmonary disease, and surgical treatment for patients with congenital heart disease and mitral stenosis. There is some evidence that the use of the bronchodilator terbutaline sulfate may decrease pulmonary vascular resistance and lessen the load of the right ventricle in patients with chronic obstructive pulmonary disease.

A variety of vasodilator drugs have been used with varying success in the treatment of primary pulmonary hypertension and other forms of pulmonary hypertension. These include tolazoline hydrochloride (25 mg every four to six hours), isoproterenol hydrochloride (10 to 20 mg sublingually every three to four hours), hydralazine hydrochloride (25 to 75 mg every six hours), diazoxide (100 to 200 mg every 8 to 12 hours) and, most recently, nifedipine (10 to 40 mg every six hours). Individual patient response is influenced by the summation of pharmacologic effects on the systemic and pulmonary circulations. These vary from person to person. Vasodilators may reduce pulmonary vascular resistance and pulmonary artery pressure may not change if the cardiac output increases as the pulmonary vascular resistance falls.

Alternatively, pulmonary artery pressure may increase in patients in whom systemic effects predominate, resulting in a fall in systemic vascular resistance and increased cardiac output without a simultaneous fall in pulmonary vascular resistance. Initiation of therapy for primary pulmonary hypertension requires heart catheterization and the careful hemodynamic assessment of individual patient response to specific drugs.

Total heart-lung transplantation has been successfully completed in victims of primary pulmonary hypertension and is an experimental form of treatment that holds promise.

To develop a better understanding of the natural history, pathophysiology and response to therapy of